

Haemolytic anaemias

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There are four causes of haemolytic anaemia that are generally amenable to splenectomy . Hereditary spherocytosis is an autosomal dominant hereditary disorder characterised by the presence of spherocytic red cells, caused by various molecular defects in the genes that code for alpha- and beta-spectrin, ankyrin, band 3 protein, protein 4.2 and other erythrocyte membrane proteins. These proteins are necessary to maintain the normal biconcave shape of the erythrocyte. Spherocytosis arises essentially from an increase in permeability of the red cell membranes to sodium. As this ion leaks into the cell, the osmotic pressure rises, resulting in swelling and increased fragility of the spherocyte. As the sodium pump has to work harder to rid the cells of sodium, there is greater loss of membrane phospholipid, resulting in an increased fragility of the membrane, and the energy and oxygen requirements increase. A large number of red cells are destroyed in the spleen, where there is a relative deficiency of both glucose and oxygen. The clinical presentation is generally in childhood but may be delayed until later life. Mild intermittent jaundice is associated with mild anaemia, splenomegaly and gallstones. Circulating bilirubin is not conjugated with glucuronic acid and is not therefore excreted in the urine as it is bound to albumin. Excretion of the resulting bilirubin complex by the liver favours formation of pigment gallstones. Once the disease manifests itself, spontaneous remissions are uncommon; the patient is often pale and jaundiced at presentation and, in established cases, lassitude and undue fatigue are present. In some families, the disease is characterised by a severe crisis of red blood cell destruction, during which the erythrocyte count may fall from $4.5 \times 10^{12}/\text{mL}$ to $1.5 \times 10^{12}/\text{mL}$ within 1 week. Such crises are characterised by the onset of pyrexia, abdominal pain, nausea, vomiting and extreme pallor, followed by increasing jaundice. These episodes may be precipitated by acute infection. Any child with gallstone disease should be investigated for hereditary spherocytosis and a family history sought. Examination reveals splenomegaly and the liver may also be palpable. Chronic leg ulcers may arise in adults. Haematological investigations include the fragility test. Erythrocytes begin to haemolyse in 0.47% saline solution but, in this condition, haemolysis may occur in 0.6% or even stronger solutions. Immature red blood cells (reticulocytes), which differ from adult cells by possessing a reticulum, are discharged into the circulation by the bone marrow to compensate for the loss of erythrocytes by haemolysis. Faecal urobilinogen is increased as this route excretes most of the urobilinogen. ⁵¹ Radioactive chromium (Cr) labelling of the patient's own red cells will demonstrate the severity of red cell destruction. Daily scanning over the spleen will show the degree of red cell sequestration by the spleen. The presence of high levels of splenic radioactivity generally predicts a good response to splenectomy . All patients with hereditary spherocytosis should be treated by splenectomy but, in juvenile cases, this is generally delayed until 6 years of age to minimise the risk of postsplenectomy sonography should be performed preoperatively to determine the presence of gallstones. Acquired autoimmune haemolytic anaemia This condition is divided into immune- and non-immune mediated forms. It may arise following exposure to agents such as chemicals, infection or drugs, e.g. alpha-methyldopa, or be associated with another disease (e.g. systemic lupus erythematosus). In most instances, the cause is unknown, and red

cell survival is reduced because of an immune reaction triggered by immunoglobulin or complement on the red cell surface. The condition is more common in women after the age of 50 years. The spleen is enlarged in about half the patients and pigment gallstones are present in about 20%. Anaemia is invariably present and may be associated with spherocytosis because of red cell membrane damage. In the immune type, antibody, which coats the red cells, can be detected by agglutination when anti-human globulin is added to a suspension of the patient's erythrocytes (Coombs' test positive). The disease runs an acute self-limiting course and no treatment is necessary. Splenectomy should, however, be considered if corticosteroids are ineffective, when the patient is developing complications from long-term steroid treatment or if corticosteroids are contraindicated; 80% of patients respond to splenectomy.

Thalassaemia (synonyms: Cooley's anaemia, Mediterranean anaemia) This condition results from a defect in haemoglobin peptide chain synthesis and is transmitted most commonly as a recessive trait. The disease is really a group of related diseases, alpha, beta and gamma, depending upon which haemoglobin peptide chain rate of synthesis is reduced. Most patients have beta-thalassaemia, in which a reduction in the rate of beta-chain synthesis results in a decrease in haemoglobin A. Intracellular precipitates (Heinz bodies) contribute to premature red cell destruction. Graduations of the disease range from heterozygous thalassaemia minor to homozygous thalassaemia major, which is associated with chronic anaemia, jaundice and splenomegaly. Patients with homozygous thalassaemia major frequently develop clinical signs in the first year of life, and these include retarded growth, enlarged head with slanting eyes and depressed nose, leg ulcers, jaundice and abdominal distension secondary to splenomegaly. Red cells are small, thin and misshapen and have a characteristic resistance to osmotic lysis. In the more severe forms, nucleated red cells and other immature blood cells are seen. The diagnosis is confirmed by haemoglobin electrophoresis. Blood transfusion may be required to correct profound anaemia, but the patient may become transfusion dependent because of hypersplenism. Splenectomy is therefore of benefit in patients who require frequent blood transfusion or if haemolytic antibodies have developed.

Robin Royston Amos Coombs, 1921–2006, Quick Professor of Biology, University of Cambridge, Cambridge, UK, described this test in 1945. Thomas Benton Cooley, 1871–1945, Professor of Pediatrics, Wayne University, Detroit, MI, USA, described this type of anaemia in 1927.

Sickle cell disease is a hereditary, autosomal recessive haemolytic anaemia occurring mainly among those of African origin, in whom the normal haemoglobin A is replaced by haemoglobin S (HbS). The HbS molecule crystallises when blood oxygen-tension is reduced, thus distorting and elongating the red cell. The resulting increased blood viscosity may obstruct the flow of blood in the spleen. Splenic microinfarcts are therefore common. The sickle cell trait can be detected in 9% of those of African origin, but most are asymptomatic; sickle cell disease occurs in about 1% of Africans. Depending upon the vessels affected by vascular occlusion, patients may complain of bone or joint pain, priapism, neurological abnormalities, skin ulcers or abdominal pain due to visceral blood stasis. The diagnosis is made by finding characteristic sickle-shaped cells on blood film, although this investigation has largely been replaced by haemoglobin electrophoresis. Hypoxia that provokes a sickling crisis should be avoided and is particularly relevant in patients undergoing general anaesthesia. Adequate hydration and partial exchange transfusion may help in a crisis. Splenectomy is of benefit in a few patients in whom excessive splenic sequestration of red cells aggravates the anaemia. Chronic hypersplenism usually occurs in late childhood or adolescence, although *Streptococcus pneumoniae* infection may precipitate an acute form in the first 5 years of life.

Revision #1

Created 2025-12-31 15:26:15 UTC by Omar Ayman

Updated 2025-12-31 15:26:15 UTC by Omar Ayman